

REMARKS

I. 2ND PRELIMINARY AMENDMENT

This amendment changes the claim identifiers to reflect the claims' current status as "withdrawn", "previously presented, *etc.* Claim 4 is amended to correct a minor clerical error that was not noticed previously. Claim 30 is amended for greater clarity, to indicate that it is the "bacterium" and not the "GI tract" that is being transformed, a point which is rather obvious from the context.

No new matter is being introduced by these amendments and their entry is respectfully requested.

II. RESPONSE TO RESTRICTION/SPECIES ELECTION REQUIREMENT

The Office Action states that the present claims comprises 5 independent inventions as follows:

- Group I: claims 1-13, 30 and 31, drawn to a method of treating a deficiency of a Hedgehog ("Hh") protein in the GI tract of a subject comprising providing to the GI tract a composition comprising a source of a Hh protein.
- Group II: claims 25 and 26, drawn to a method of determining whether a subject is at risk for developing a GI tract tumor comprising measuring the level of Hh protein or mRNA in a GI tract tissue sample.
- Group III: claim 27, drawn to a method of diagnosing the presence of ectopic gastric tissue, or susceptibility of developing such, by determining the level of Hh, BMP2 or BMP4 mRNA.
- Group IV: claims 28 and 29, drawn to a therapeutic composition comprising a nucleic acid in the form of an expression vector encoding a Hh or an enteric bacterium comprising the nucleic acid sequence.
- Group V: claims 32 and 33, drawn to a method for preventing development of, or treating, a disease or condition characterized by the presence or growth a Hh protein-expressing ectopic gastric tissue in a subject, comprising providing to the subject an effective amount of a substance that reduces the functional level or activity of the Hh protein.

The Office alleges that the inventions listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The ISA/US considers that where multiple products are claimed, the main invention shall consist of the first invention of the category first mentioned in the claims and the first recited invention of each of the other categories related thereto. Accordingly, here, the "main invention" would consist of the first method (Group I) and the first (and only) claimed product used in this method (the composition of Group IV). The technical feature linking groups I and IV is said to be the a composition comprising a nucleic acid and methods of treatment using that composition.

According to the Action, the cited prior art (Ingham *et al.* U.S. Pat .6,165,747, published 12/26/00, discloses a composition encompassed by the composition of Group IV. Specifically, this reference allegedly teaches compositions comprising an expression vector comprising a nucleic acid encoding a Hh protein. According to the Action, Ingham states:

"...the present invention relates to nucleic acids encoding vertebrate hedgehog proteins... and preparations of such compositions"

(col. 16, lines 21-26) and

"...expression constructs of the subject vertebrate hh polypeptide, and mutants thereof, may be administered in any biologically effective carrier, e.g. any formulation or composition capable of effectively delivering the recombinant gene to cells in vivo"

(col. 26, lines 35-39).

The Action concludes that because Group IV reads on such compositions, the technical feature linking Groups I and IV does not constitute a special technical feature as defined by the PCT rules because it does not define a contribution over the prior art. (Applicant will not reiterate here the Office's statements regarding Groups II, III and V).

Applicants' Response to the Restriction Requirement

Applicants do not agree with the Office's interpretation of the cited reference in relation to the pending claims (such as those of Group I and IV), and believe that Groups I and IV should be rejoined as a single invention. Applicants nevertheless elect, with traverse, Group I, claims 1-13, 30 and 31 for examination at this time.

ELECTIONS OF SPECIES and APPLICANTS' ELECTION

The Office has further required an election of species as described below.

A. First Species Election Requirement

In the case of Group I (which is being elected herein), Applicants were required to elect one species representing of a source of a Hedgehog protein of the generic invention.

- (1) Hedgehog protein (including homologues and variants of said protein);
- (2) nucleic acid expression vector;
- (3) enteric bacteria capable of colonizing the GI tract that expresses and secretes Hedgehog protein;
- (4) animal cell that expresses and secretes Hedgehog protein; and
- (5) molecule or agent that induces or upregulates Hedgehog protein.

According to the Office, the following claims were considered to be generic, or to read on the various species. (Comments below are limited to species falling within Group I.)

1. *Claims 1-7 are generic.*
2. *Claims 8, 9, 30 and 31 correspond to each species* (Applicants' believe that the intention here was to state that claims 8, 9, 30 and 31 cover "all" the species in the above list.)
3. *Claims 10 and 11 correspond to species (1) above – the Hh protein.*
4. *Claim 12 corresponds to species (2) above, the nucleic acid.*
5. *Claim 13 corresponds to species (3), the enteric bacterium*

Applicants' First Species Election

Applicants hereby elect Species A (2): nucleic acid expression vector. Applicants believe that the following claims read on this first elected species: Claims 1-9, 12, 30 and 31.

B. Second Species Election Requirement

In the case of Group I (which is being elected herein), Applicants were required to elect one species of cancer from the following list:

- (1) gastric cancer,
- (2) colon (large intestinal) cancer,
- (3) small intestinal cancer, and
- (4) esophageal cancer.

According to the Office, the following claims were considered to be generic and read on the various species. The discussion here is limited to species falling within Group I.

1. *Claims 1, 2, 4, 6, 10-13, 30 and 31 are generic.*
2. *Claims 3 and 5 each correspond to two species of gastric (species 1) and colon cancer (species 2) .*
3. *Claims 7-9 are considered to correspond to colon cancer because these claims are directed to "familial adenomatous polyposis coli" (FAP), which leads to colon cancer.*

Applicants' Second Species Election

Applicants hereby elect Species B (2): colon (large intestinal) cancer for initial examination.

Applicants believe that all the elected claims, claims 1-13 and 30-31, read on this second elected species.

Thus, the claims that are either generic to, or read on, BOTH elected species are claims 1-9, 12, 30 and 31.

Applicants understand that once claims examined in a manner that is limited to the elected species are found to be allowable, the search and examination will be extended to the additional species up to and including the genus.

III. CONCLUSION

Applicants respectfully request entry of the foregoing claims as amended and response reconsideration of the restriction requirement as discussed. . The application is now in condition for Examination on the merits and allowance.

Respectfully submitted,
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